

PA-IDC

QUERY CONTROL FORM		RTIS USE ONLY	
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Examiner-GAU <u>Killios</u>	Date <u>4/22/04</u>	Week Date <u>02-09-04</u>	
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JACKET			
a. Serial No.	f. Foreign Priority	k. Print Claim(s)	p. PTO-1449
b. Applicant(s)	g. Disclaimer	l. Print Fig.	q. PTOL-85b
c. Continuing Data	h. Microfiche Appendix	m. Searched Column	r. Abstract
d. PCT	i. Title	n. PTO-270/328	s. Sheets/Figs
e. Domestic Priority	j. Claims Allowed	o. PTO-892	t. Other

SPECIFICATION	MESSAGE
a. Page Missing	<p>Please supply Brief Description of Drawings paragraph in specification.</p> <p>Thank you</p> <p>ewc</p>
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CLAIMS	
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	RESPONSE <u>Please see p. 13 for Figure 1</u>
	<u>and page 14 for Figure 2.</u>
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	initials <u>CT</u>

Example 3 - Intraocular pressure (IOP) studies after single dose in rabbits with water-increased IOP.

A study versus placebo was carried out in 20 New-Zealand albino rabbits to evaluate the effects of CHF 1035 after single administration. Basal intraocular pressure (IOP) was measured in anaesthetized rabbits in both eyes. Each eye received two drops of physiological solution containing 5% of the drug. Control animals received only physiological solution. After one hour, the animals were administered by oral route with a total amount of 200 ml of distilled water. IOP increased within about one hour and normalized after about 3 hours. As no differences in IOP were observed between the two eyes, the respective tonometric curves were superimposed. IOP measurements were carried out by using a Goldman tonometer and were repeated one hour after the administration of water.

Figure 1 shows the effect of CHF 1035 on rabbit intraocular pressure (IOP) after water loading. Values are expressed as mean ( $SE^1 = 1.6-2.7$ ). The total number of eyes per group is in brackets.

It can be appreciated that the animals pre-treated with CHF 1035 show an IOP value significantly lower than control animals.

<sup>1</sup> Standard error

Example 4 - Intraocular pressure (IOP) studies after repeated administration in rabbits with water-increased IOP.

The effectiveness of CHF 1035 after repeated administration was tested in a study versus placebo, in 20 New-Zealand albino rabbits. In order to induce a chronic increase of the IOP, each animal was intraocularly injected with 0.5 mg/day of  $\alpha$ -chymotrypsin for five days. Starting from the first day of treatment, two drops of physiological

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saline containing 5% of the drug were instilled in each eye every 6 hours. The control animals only received physiological saline.

5 The IOP measurement was performed as described in example 1, before the injection and subsequently every day until the 10<sup>th</sup> day.

Figure 2 reports the effect of CHF 1035 on rabbit IOP after  $\alpha$ -chymotrypsin injection. Values are reported as mean (SE = 1.2 -2.6; n = 20 per group).

10 IOP values are similar before the injection of  $\alpha$ -chymotrypsin. However, the animals treated with CHF 1035 showed significantly lower IOP than animals treated with placebo. Moreover, the medicament turned out to be well tolerated during the whole cycle of treatment and induced  
15 no eye irritation and/or discomfort.